

P ENT COOPERATION TREA

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

STEWART, Michael, I.
Sim & McBurney
6th floor
330 University Avenue
Toronto, Ontario M5G 1R7
CANADA

Date of mailing (day/month/year) 03 August 2001 (03.08.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 1038-1024 MIS:sd	
International application No. PCT/CA00/00227	International filing date (day/month/year) 03 March 2000 (03.03.00)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input type="checkbox"/> the inventor	<input type="checkbox"/> the agent <input type="checkbox"/> the common representative
Name and Address CONNAUGHT LABORATORIES LIMITED 1755 Steeles Avenue West Toronto, Ontario M2R 3T4 Canada	State of Nationality CA	State of Residence CA
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input type="checkbox"/> the person	<input checked="" type="checkbox"/> the name	<input type="checkbox"/> the address <input type="checkbox"/> the nationality <input type="checkbox"/> the residence
Name and Address AVENTIS PASTEUR LIMITED 1755 Steeles Avenue West Toronto, Ontario M2R 3T4 Canada	State of Nationality	State of Residence
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer: J. Leitao
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

TENT COOPERATION TRE, /

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 12 January 2001 (12.01.01)	
International application No. PCT/CA00/00227	Applicant's or agent's file reference 1038-1024
International filing date (day/month/year) 03 March 2000 (03.03.00)	Priority date (day/month/year) 05 March 1999 (05.03.99)
Applicant LI, Xiaomao et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

03 October 2000 (03.10.00)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland

Authorized officer

R. E. Stoffel

Facsimile No. (41-22) 740.14.35

Telephone No. (41-22) 338.83.38

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

RECEIVED

MAR 28 2001

PCT

SIM & MCBURNEY
HUGHES, ASHTON & MCKAY

To:

Stewart, Michael, T.
Sim & McBurney
330 University Avenue
6th Floor
Suite 600
Toronto, Ontario M5G 1R7
CANADA

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing

(day/month/year)

22.03.2001

Applicant's or agent's file reference

1038-1024 MIS

IMPORTANT NOTIFICATION

International application No.

PCT/CA00/00227

International filing date (day/month/year)

03/03/2000

Priority date (day/month/year)

05/03/1999

Applicant

CONNAUGHT LABORATORIES LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Emslander, S



Tel. +49 89 2399-8718



PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 1038-1024 MIS	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/CA00/00227	International filing date (day/month/year) 03/03/2000	Priority date (day/month/year) 05/03/1999
International Patent Classification (IPC) or national classification and IPC C12N15/45		
Applicant CONNAUGHT LABORATORIES LIMITED et al.		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none">I <input checked="" type="checkbox"/> Basis of the reportII <input type="checkbox"/> PriorityIII <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicabilityIV <input type="checkbox"/> Lack of unity of inventionV <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statementVI <input type="checkbox"/> Certain documents citedVII <input type="checkbox"/> Certain defects in the international applicationVIII <input checked="" type="checkbox"/> Certain observations on the international application		
Date of submission of the demand 03/10/2000	Date of completion of this report 22.03.2001	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel.: +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Roscoe, R Telephone No. +49 89 2399 2554 	

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA00/00227

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):*

Description, pages:

1-43 as originally filed

Claims, No.:

1-24 as originally filed

Drawings, sheets:

1/39-39/39 as originally filed

Sequence listing part of the description, pages:

1-8, filed with the letter of 26.05.00

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA00/00227

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:
see separate sheet

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 1-24
	No:	Claims
Inventive step (IS)	Yes:	Claims
	No:	Claims 1-24
Industrial applicability (IA)	Yes:	Claims 1-11, 22-24
	No:	Claims 12-21

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

I. Basis

The documents mentioned in the present International Preliminary Examination Report are numbered as in the search report, i.e. D1 corresponds to the first document of the search report etc.

V. Reasoned statement on Novelty, Inventive Step and Industrial Applicability

- Novelty (Art.33(2) PCT)

None of the cited prior art documents provide an enabling disclosure against novelty of present claims.

- Inventive Step (Art.33(3) PCT)

The problem addressed by the present invention is to eliminate the need for cardiotoxin pretreatment prior to immunization with DNA-F vectors. This problem had already been identified in D1 (p.684). The solution is the use of heterologous (preferably HSV I gD) signal sequence. D1 (closest prior art) discloses that the cardiotoxin pretreatment step can be eliminated using a more effective signal peptide (p.684, Col.2, l.5-8). Hence, although D1 does not state which sequence to use, and is thus not considered sufficiently enabling to form the basis for a novelty objection, D1 does disclose the principle underlying the present application. In putting the teaching of D1 into practice, a skilled person would test heterologous signal sequences which have been shown to be beneficial in other nucleic acid vaccines in the prior art. D2 demonstrates the use of HSV I gD signal in the context of HCV DNA vaccines. The gD signal had previously been successfully been used to enhance expression / secretion in the context of HIV-1 vectors (p.446, bottom col.1). Hence, D1 in combination with D2 renders even the preferred embodiment of the present application non-inventive. D1 in combination with D4 also can be considered to render the present claims non-inventive, since D4 demonstrates replacement of signal sequence in an RSV G protein vector (the specific embodiment cited is human tissue plasminogen activator signal - which could well also achieve improved expression over the autologous signal in the present case).

All specific embodiments relate to above concept and are trivial workshop modifications that can be found in analogous RSV G protein application D4.

Hence, present application totally devoid of inventive subject-matter.

- **Industrial Applicability (Art.33(4) PCT)**

For the assessment of the present claims 12-21 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Claims 12-21 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

VIII. Certain observations

- **Clarity (Art.6 PCT)**

Claims 10, 21 and 23 comprise reference to p82M35B which is an arbitrary definition. All claims referring to this plasmid must qualify the term by reference to ATCC deposit 203790 and preferably also by reference to Fig.10.

Claim 24 - Product-by-process claim format not allowable.

The claims are considered unsupported by the description in their present breadth. Applicant has only shown the beneficial properties of one specific heterologous signal sequence. He has not shown that a specific type of signal sequence (having e.g. a particular feature) is beneficial so the skilled person is provided with absolutely no guidance as to whether any other signal sequences

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/CA00/00227

could be of use. Hence, the claims should be limited to vectors having the HSV1 gD signal sequence.

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

To:
Sim & McBurney
Attn: Stewart, Michael, T.
330 University Avenue
6th Floor
Toronto, Ontario M5G 1R7
CANADA

Date of mailing
(day/month/year) 07/09/2000

Applicant's or agent's file reference
1038-1024

FOR FURTHER ACTION See paragraphs 1 and 4 below

International application No.
PCT/CA 00/00227

International filing date
(day/month/year) 03/03/2000

Applicant

CONNAUGHT LABORATORIES LIMITED et al.

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
Fax: (+31-70) 340-3016

Authorized officer

Andria Overbeeke-Siepkens

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 1038-1024	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/CA 00/ 00227	International filing date (day/month/year) 03/03/2000	(Earliest) Priority Date (day/month/year) 05/03/1999
Applicant CONNAUGHT LABORATORIES LIMITED et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows.

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☒ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

1

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No.

/CA 00/00227

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/45 A61K39/155 A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols):

IPC 7 C07K C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used):

MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category ²	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>LI X ET AL: "Protection against respiratory syncytial virus infection by DNA immunization"</p> <p>THE JOURNAL OF EXPERIMENTAL MEDICINE, vol. 188, no. 4, 17 August 1998 (1998-08-17), pages 681-688, XP002145604</p> <p>ISSN/ISBN:0022-1007</p> <p>the whole document</p> <p style="text-align: center;">--- -/--</p>	1-24



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

¹ Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

24 August 2000

Date of mailing of the international search report

07/09/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel: (+31-70) 340-2040, Tx: 31 651 epcnl,
 Fax: (+31-70) 340-3016

Authorized officer

Cupido, M

INTERNATIONAL SEARCH REPORT

International Application No

T/CA 00/00227

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	LEE SW ET AL: "Hepatitis C virus envelope DNA-based immunization elicits humoral and cellular immune responses" MOLECULES AND CELLS, vol. 8, no. 4, 31 August 1998 (1998-08-31), pages 444-451, XP000938576 ISSN-ISBN:1016-8478 page 446, left-hand column, last paragraph; figure 1 ---	1-24
Y	WO 96 40945 A (CONNAUGHT LABORATORIES LIMITED) 19 December 1996 (1996-12-19) cited in the application the whole document ---	1-24
A	WO 99 04010 A (CONNAUGHT LABORATORIES LIMITED) 28 January 1999 (1999-01-28) page 34, line 14 - line 22 -----	1,4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 00/00227

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 12-21 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

T/CA 00/00227

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
W0 9640945 A	19-12-1996	US 6019980 A	01-02-2000
		AU 695527 B	13-08-1998
		AU 6117696 A	30-12-1996
		BR 9608615 A	15-06-1999
		CA 2223610 A	19-12-1996
		EP 0832253 A	01-04-1998
		JP 11507808 T	13-07-1999
		US 6083925 A	04-07-2000
		US 5843913 A	01-12-1998
		US 5880104 A	09-03-1999
		US 6017897 A	25-01-2000
		US 6022864 A	08-02-2000
W0 9904010 A	28-01-1999	AU 8427898 A	10-02-1999
		EP 0996730 A	03-05-2000

PCT

WIPO

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT



(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 1038-1024 MIS	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/CA00/00227	International filing date (day/month/year) 03/03/2000	Priority date (day/month/year) 05/03/1999
International Patent Classification (IPC) or national classification and IPC C12N15/45		
Applicant CONNAUGHT LABORATORIES LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

I	<input checked="" type="checkbox"/>	Basis of the report
II	<input type="checkbox"/>	Priority
III	<input type="checkbox"/>	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	<input type="checkbox"/>	Lack of unity of invention
V	<input checked="" type="checkbox"/>	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	<input type="checkbox"/>	Certain documents cited
VII	<input type="checkbox"/>	Certain defects in the international application
VIII	<input checked="" type="checkbox"/>	Certain observations on the international application

Date of submission of the demand 03/10/2000	Date of completion of this report 22.03.2001
Name and mailing address of the international preliminary examining authority  European Patent Office D-80298 Munich Tel: +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Roscoe, R Telephone No. +49 89 2399 2554 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA00/00227

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:

Description, pages:

1-43 as originally filed

Claims, No.:

1-24 as originally filed

Drawings, sheets:

1/39-39/39 as originally filed

Sequence listing part of the description, pages:

1-8, filed with the letter of 26.05.00

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

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- ☒ furnished subsequently to this Authority in written form.
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- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

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- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:
see separate sheet

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-24
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-24
Industrial applicability (IA)	Yes:	Claims	1-11, 22-24
	No:	Claims	12-21

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

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I. Basis

The documents mentioned in the present International Preliminary Examination Report are numbered as in the search report, i.e. D1 corresponds to the first document of the search report etc.

V. Reasoned statement on Novelty, Inventive Step and Industrial Applicability

- Novelty (Art.33(2) PCT)

None of the cited prior art documents provide an enabling disclosure against novelty of present claims.

- Inventive Step (Art.33(3) PCT)

The problem addressed by the present invention is to eliminate the need for cardiotoxin pretreatment prior to immunization with DNA-F vectors. This problem had already been identified in D1 (p.684). The solution is the use of heterologous (preferably HSV I gD) signal sequence. D1 (closest prior art) discloses that the cardiotoxin pretreatment step can be eliminated using a more effective signal peptide (p.684, Col.2, l.5-8). Hence, although D1 does not state which sequence to use, and is thus not considered sufficiently enabling to form the basis for a novelty objection, D1 does disclose the principle underlying the present application. In putting the teaching of D1 into practice, a skilled person would test heterologous signal sequences which have been shown to be beneficial in other nucleic acid vaccines in the prior art. D2 demonstrates the use of HSV I gD signal in the context of HCV DNA vaccines. The gD signal had previously been successfully been used to enhance expression / secretion in the context of HIV-1 vectors (p.446, bottom col.1). Hence, D1 in combination with D2 renders even the preferred embodiment of the present application non-inventive. D1 in combination with D4 also can be considered to render the present claims non-inventive, since D4 demonstrates replacement of signal sequence in an RSV G protein vector (the specific embodiment cited is human tissue plasminogen activator signal - which could well also achieve improved expression over the autologous signal in the present case).

All specific embodiments relate to above concept and are trivial workshop modifications that can be found in analagous RSV G protein application D4.

Hence, present application totally devoid of inventive subject-matter.

- **Industrial Applicability (Art.33(4) PCT)**

For the assessment of the present claims 12-21 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Claims 12-21 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

VIII. Certain observations

- **Clarity (Art.6 PCT)**

Claims 10, 21 and 23 comprise reference to p82M35B which is an arbitrary definition. All claims referring to this plasmid must qualify the term by reference to ATCC deposit 203790 and preferably also by reference to Fig.10.

Claim 24 - Product-by-process claim format not allowable.

The claims are considered unsupported by the description in their present breadth. Applicant has only shown the beneficial properties of one specific heterologous signal sequence. He has not shown that a specific type of signal sequence (having e.g. a particular feature) is beneficial so the skilled person is provided with absolutely no guidance as to whether any other signal sequences

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could be of use. Hence, the claims should be limited to vectors having the HSVI
gD signal sequence.